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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/279,275	07/22/1994	HOWARD L. WEINER	101016104US1	7626

7590 12/02/2002

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82

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/279,275	Applicant(s) Weiner et al.
	Examiner G.R. Ewoldt	Art Unit 1644
-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --		
Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.		
- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).		
Status		
1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>Sep 19, 2002</u>		
2a) <input checked="" type="checkbox"/> This action is FINAL. 2b) <input type="checkbox"/> This action is non-final.		
3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11; 453 O.G. 213.		
Disposition of Claims		
4) <input checked="" type="checkbox"/> Claim(s) <u>29, 31-33, 35, 37, 38, and 40</u> is/are pending in the application.		
4a) Of the above, claim(s) _____ is/are withdrawn from consideration.		
5) <input type="checkbox"/> Claim(s) _____ is/are allowed.		
6) <input checked="" type="checkbox"/> Claim(s) <u>29, 31-33, 35, 37, 38, and 40</u> is/are rejected.		
7) <input type="checkbox"/> Claim(s) _____ is/are objected to.		
8) <input type="checkbox"/> Claims _____ are subject to restriction and/or election requirement.		
Application Papers		
9) <input type="checkbox"/> The specification is objected to by the Examiner.		
10) <input type="checkbox"/> The drawing(s) filed on _____ is/are a) <input type="checkbox"/> accepted or b) <input type="checkbox"/> objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).		
11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.		
12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.		
Priority under 35 U.S.C. §§ 119 and 120		
13) <input type="checkbox"/> Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) <input type="checkbox"/> All b) <input type="checkbox"/> Some* c) <input type="checkbox"/> None of: 1. <input type="checkbox"/> Certified copies of the priority documents have been received. 2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____. 3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). *See the attached detailed Office action for a list of the certified copies not received.		
14) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e). a) <input type="checkbox"/> The translation of the foreign language provisional application has been received.		
15) <input checked="" type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.		
Attachment(s)		
1) <input type="checkbox"/> Notice of References Cited (PTO-892)		
4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____		
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)		
5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)		
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____		
6) <input type="checkbox"/> Other: _____		

DETAILED ACTION

1. Claims 29, 31-33, 35, 37-38, and 40 are pending and being acted upon.
2. Applicant's submission of formal drawings is acknowledged. It was an oversight on the Examiner's part not to indicate in the previous action that a Form 948 was first mailed as part of Paper No. 8, mailed 10/01/91.
3. In view of Applicant's amendment, filed 9/19/02, only the following rejections remain.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 29, 31-33, 35, 37-38, and 40 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for,

a method for the treatment of myelin basic protein (MBP) induced experimental allergic encephalomyelitis (EAE) in Lewis rats, and a method for the treatment of adjuvant induced arthritis (AA) in Lewis rats, does not reasonably provide enablement for,

a method for the treatment of a T cell-mediated or T cell-dependent autoimmune disease by suppressing an autoimmune response associated with said disease in a human presenting with said autoimmune response, said method comprising orally or enterally administering to said human at least one antigen in an amount effective to suppress said autoimmune response, said antigen selected from the group consisting of autoantigens specific for said autoimmune disease, said suppression comprising elicitation of suppressor T cells specific to said administered antigen, or

a method of treating a T cell-mediated or T cell-dependent autoimmune disease by suppressing an autoimmune response associated with said disease in a human presenting with said autoimmune response, said method comprising orally or enterally administering to said human at least one antigen in an amount effective to suppress said autoimmune response said antigen selected from the group consisting of autoantigens specific for

said autoimmune disease, for the reasons of record as set forth in Paper No. 78, mailed 3/19/02.

Applicant's arguments, filed 9/19/02, have been fully considered but they are not persuasive. Applicant argues that "The present claims are clearly limited to (I) treatment by suppression of an autoimmune response; and (ii) autoimmune responses associated with T-cell mediated or T-cell dependent autoimmune diseases. Therefore, the present claims clearly exclude poison ivy and do not require a cure or even an improvement of such clinical parameters as are measured in a Phase III clinical study."

Regarding poison ivy, the poison ivy delayed type hypersensitivity response is T cell mediated and can be considered an autoimmune response. Accordingly, a treatment for said response would be encompassed by the claims. Said treatment by the methods of the instant claims remains highly unpredictable.

Applicant argues that the two Phase III clinical trials of record, in which oral tolerance failed both times, should not be relied upon as the trials did not measure the abatement of an abnormal autoimmune response, i.e., the method of the instant claims. Applicant cites Weiner et al. (*Science*, 1993, of record) in support of the method of the instant claims.

Applicant is reminded that the method of the instant claims recites a treatment for a human, T cell-mediated autoimmune disease, in particular, MS. It is the Examiner's position that the method of the instant claims must be enabled for its intended use, i.e., the treatment of a human, T cell-mediated autoimmune disease, in particular, MS. The evidence of record, i.e., the failure of both collagen and MBP in human clinical trials for the treatment of the human, T cell-mediated autoimmune diseases rheumatoid arthritis and MS, respectively, indicates that the method of the instant claims does not work for its intended use. Additionally, it is noted that in the Weiner et al. reference, parameters such as EDSS score and exacerbation (attack frequency) were measured, just as in the Phase III study of MBP for the treatment of MS. Weiner et al. found that "It must be strongly emphasized that this study does not demonstrate efficacy of oral myelin in the treatment of MS." Thus, of record, we have two failed human studies and one inconclusive one. Accordingly, it remains the Examiner's position that the method of the instant claims is at best, highly unpredictable.

Applicant's arguments indicate a number of reasons why clinical studies might fail, however, Applicant provides no evidence that the studies of record failed for any reason other than that which must be considered most likely, the simple fact that the method of the instant claims did not work. Accordingly, it is unclear how this evidence supports the method of the instant claims.

Applicant argues that the *In re Wands* factors "are a mere abstraction." It is the Examiner's position that abstraction or not, they are the factors by which the enablement of any particular invention is examined.

Applicant argues that "The Examiner has also dismissed the applicants' discussion of what the experiments described in the Examples of the specification conveyed to a person of ordinary skill in the art at the time, and what these experiments were designed to demonstrate by those who designed them at the time, and what these experiments were designed to demonstrate by those who designed them at the time."

The Examiner has not dismissed Applicant's discussion, the Examiner has merely found that the discussion, and evidence of record, is insufficient to support a method for the treatment of a T cell-mediated autoimmune disease in a human. The evidence of record indicates that Applicant's method might function in a number of animal models. Accordingly, the method disclosed in the specification has been found enabled for certain animal uses. The evidence of record also indicates that the method of the instant claims have failed in at least two human trials. Given that the instant claims are drawn to a method for treating humans, the human data must be found the most compelling. Therefore, it remains the Examiner's position that the method of the instant claims must be considered at best, highly unpredictable.

Applicant concludes with an argument/discussion of the mechanisms by which oral tolerance might function.

It is the Examiner's position that said mechanisms are irrelevant as the methods of the instant claims have so far proven to be non-functional in humans.

6. The following are new grounds of rejection necessitated by Applicant's amendment.

7. Claims 29, 31-33, 35, 37-38, and 40 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) a method for the treatment of a T cell-mediated or T cell-dependent autoimmune disease by suppressing an autoimmune response associated with said disease in a human presenting with said autoimmune response (Claims 29 and 35),

B) a method of treating MS comprising administering an autoantigen, wherein said autoantigen is bovine myelin basic protein (Claim 37).

Applicant's amendment, filed 9/19/02, fails to assert that no new matter has been added. Regarding A), the specification repeatedly states that the methods of the instant claims comprise a method for the treatment of an autoimmune disease, however, no support has been found for a method of treating an autoimmune response in a patient presenting with said response. Indeed a review of the Examples indicates that in most cases the treatment is administered before the induction of the disease, thus, there was no treatment after presentation. Regarding B), Applicant asserts that support for Claim 37 can be found in Example 6, at page 21 of the specification. Said example does not provide support for treating MS by administering bMBP. Said example merely discloses that bMBP can inhibit the induction of EAE in rats if fed to said rats before the induction of disease.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claim 37 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9, 14, 19, and 24 of U.S. Patent No. 5,869,054. Although the conflicting claims are not identical, they are not patentable distinct from each other because the claims recite a method of treating MS in a human comprising administering to said human MBP. Note that instant Claim 37 recites bovine MBP whereas the claims of the '054 patent recite generic MBP. However, the specifications disclose just two species of MBP, guinea pig and bovine. Accordingly, the administration of either MBP would be obvious.

10. Claim 37 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of U.S. Patent No. 6,036,957. Although the conflicting claims are not identical, they are not patentable distinct from each other because the claims recite a method of treating MS in a human comprising administering to said human an MBP autoantigen. Again note that instant Claim 37 recites bovine MBP whereas the claims of the '054 patent recite generic MBP. However, the specifications disclose just two species of MBP, guinea pig and bovine. Accordingly, the administration of either MBP would be obvious.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the

statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 at (703) 305-3014.

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November 19, 2002

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